# AMERICAN JOURNAL OF PHARMACY

★ AND THE SCIENCES SUPPORTING PUBLIC HEALTH ★

HON. HARRY J. ANSLINGER
Procter Medalist 1953
(see p. 43)

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# AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825





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CONTENTS

# E D I T O R I A L

## PRODUCT DUPLICATION

IN the many discussions and debates on the problem of substitution among retail pharmacists the matter of the multiplicity of brands has received considerable attention. Pharmacists, by and large, are concerned over their inability to stock every brand of every prescription item released by manufacturers. That this concern is well-founded is evident when the number of duplicate brands of the same drug is surveyed. The ridiculous extreme seems to have been reached in the case of isonicotinic acid hydrazide. This is supplied by thirty-eight companies, and under a different brand name in almost every instance. Obviously, no sensible pharmacist would, or could, stock so many brands if his inventory was to be kept within proper bounds. Many other similar examples could be cited such as those in the field of penicillin and triple sulfonamide products.

Many pharmacists, unfortunately, have tried to solve this problem by the simple expedient of ignoring all brand names even when these are specified on prescription. This approach is not only open to serious question on legal grounds but it involves the great risk of incurring the displeasure of the prescribing physician. Most Americans, including pharmacists and physicians, are brand conscious. We insist on our favorite brand of cigarettes, coffee, bread, shirts, hats and so on *ad infinitum*. Physicians, as well as pharmacists, know full well that not all manufacturers operate with the same quality of performance from the standpoint of care, precision and control. There are, furthermore, some companies whose policies in drug distribution, pricing, research or trade relations are not such that the physician wishes to patronize or support them. This, indeed, is his prerogative —to specify a brand and be sure his patient gets it. Pharmacists, themselves, would be highly indignant if the wholesaler were to substitute one brand for another specified on order. Surely the physician deserves the same consideration by the pharmacist.

Another solution to the duplicate brand problem often proposed by pharmacists is the establishment of some governmental restriction on the number of brands of any given drug placed upon the market.

On the surface this sounds good but further study will show otherwise. In this country we all operate on the system of free enterprise. If the government usurps such power that it can restrict the number of brands of a product permitted it can just as well decide who may and may not engage in business even in retail pharmacy. Pharmacists themselves would be the first to object to any such curtailment of their own liberties. There has been already too much invasion of individual rights by the over-zealous, professional "do-gooders" who infested Washington over the past two decades. The current program of lifting many government controls is providing a much needed reform.

It is our system of free enterprise and competition which has made our list and supply of medicinals the envy and the standard for the world. Without the stimulus offered by the opportunity for profit our whole program of drug research, development and distribution would stagnate. The retail pharmacist and specifically the prescription pharmacist has no just complaint for the level of his return over the past decade. He has prospered in proportion to others in the field, in spite of the statements to the contrary by some few malcontents.

Pharmacists must not expect to have the few inconvenient parts of our system extirpated without causing the complete breakdown of the entire system. Possibly they prefer the operation of a government bureaucracy such as that in England. Here every effort is made to reduce duplication and brand names but the catch is the mark-up—less than 20 per cent! This is even more unpopular to English pharmacists and more of a problem to them than duplicate brands is to us. Surely all of us know full well that in any life situation we must take the bitter with the sweet.

Pharmacists do have a way out of the dilemma posed by the multiplicity of brands. No reasonable physician objects when permission is asked to substitute one well known brand of a drug for another. Actually, he appreciates the professional and moral integrity of the pharmacist who sees fit to request such authorization. The physician does expect that another *well known* brand will be suggested and not a product made by some obscure manufacturer or one known to "cut corners" and sell on "price" only. It is pre-eminently unfair for the pharmacist to suggest a brand he himself would be unwilling to use if he were the patient. In drug selection there should be no "double standard".

No manufacturer objects to brand substitution providing the physician approves the change in advance and providing the substi-

tute item is an honest product standing on its own merits. He does object when the product is an out and out copy of his brand in color, shape and often even in trade name. These imitation or counterfeit products are dishonest attempts not to compete with some well known product but to be used illegitimately and by subterfuge. Almost invariably they are substituted for the genuine item without the physician's or patient's knowledge. This latter type of substitution is not only illegal and immoral but it threatens the professional integrity and reputation of all pharmacists, innocent as well as guilty.

Pharmacists should look at the problem of brand duplication objectively and cope with it in a way that is honest and fair to all concerned. While manufacturers must operate on the plane of free enterprise and competition some self-restraint in "me-tooism" should be exercised. Neither pharmacist nor manufacturer can prosper without the other and their interests are hopelessly entwined and interdependent. The recognition of this truth is the key to many of our current problems.

L. F. Tice

## PRESENTATION OF PROCTER AWARD TO HON. HARRY J. ANSLINGER, FEBRUARY 5, 1953

**By Charles E. Vanderkleed**

ON a previous occasion when it was my privilege to present the Procter Medal Award, I remarked that like Russell H. Conwell's hero who found "acres-of-diamonds" in his own back yard, so had the Philadelphia Drug Exchange found it unnecessary to go beyond the immediate Philadelphia area to select recipients for this honor. Tonight, we break that precedent only a "wee bit" by extending our area to include the great State of Pennsylvania, where in Altoona, on May 20, 1892, there was born to Robert J. and Christina Anslinger a son who was destined to play a tremendously important role in the service of his country, and in the uplift of the moral and physical welfare of humanity in the whole world.

This evening, my assignment has been rendered particularly difficult because of the necessity for my selecting only a few of the most outstanding accomplishments from a magnificent record of masterful achievements, the appropriate recounting of which would consume far more time than that allotted to me for this presentation.

I have often wondered why, in the course of human progress, the advent of an epoch making discovery or invention has had to have bound up in it a tremendous power for both good and evil. Our most recent example, atomic energy, may mean either the destruction of modern civilization or the ultimate achievement of "Peace on Earth—Good Will Toward Men." Perhaps the good Lord intended it that way in order that we might develop our moral fibre, and in order to teach us to so conduct ourselves that good may overcome all evil.

And so it was with the advent of the discovery and development of narcotic drugs,—on the one hand one of the most beneficent and life-saving achievements in the history of medicine, and on the other hand, one of the most insidious and damnable body and soul destroying agents of all time. It is primarily because of Mr. Anslinger's tremendous influence in the course of this narcotic problem that the Philadelphia Drug Exchange tonight honors itself by extending its Procter Award to our honored guest, for he has rendered incalculable

service not only in the cause of reduction of narcotic addiction the world over, but also in the maintenance of an adequate supply to care for the medical needs of our beloved country.

All too briefly may I outline the steps which led to Mr. Anslinger's greatest achievements in combatting the narcotic evil. A graduate of Pennsylvania State College and of the School of International Relations in The Hague, he attended the Washington College of Law where he received the degree of Bachelor of Laws. Then followed a thirteen year period of distinguished diplomatic service, which included, among other assignments,—Attaché of the American Legation in The Hague; American Vice-Consul in Hamburg, Germany; Consul in LaGuaira, Venezuela, and in Nassau, Bahamas; Delegate to the Conference on Suppression of Smuggling in London and Paris; to the International Congress against Alcoholism in Antwerp; and to the Conference in Ottawa to revise the Canadian Treaty with the United States.

This diplomatic training and experience stood Mr. Anslinger in good stead when in 1930 he became the first (and only) U. S. Commissioner of Narcotics in the Treasury Department, and in 1946, United States Representative on the United Nations Commission on Narcotic Drugs. Time does not permit me to enumerate all of the many accomplishments of our Commissioner during the 22 years he has held this distinguished office. However, to mention only one or two: In 1931, as United States Delegate to the League of Nations, he led the fight and succeeded in securing the adoption of a convention to limit the manufacture of narcotic drugs to the medical needs of the world. By this convention, the manufacture of morphine was reduced from 100 tons to 40 tons annually, and drug addiction declined throughout the world.

Another outstanding personal accomplishment in particular relates to the effective agreement which he secured during World War II with Great Britain, France, The Netherlands and Portugal to close down their Far Eastern monopolies where opium was sold over-the-counter. The United States had advocated and asked for this ever since 1909, but for 34 years had been repeatedly thwarted in their effort. An agreement reached in the 1912 Hague Convention was never carried out and in 1925, the American Delegation walked out of the League of Nations Conference.

Undaunted by this obstinate record, our Commissioner took up this challenge personally, and by his persuasive and diplomatic ability

succeeded in 1943 in concluding an agreement with these nations to close these monopolies. It left his international colleagues stunned by the victory, but not without their grateful acknowledgment of his leadership. Sir Leonard Lyall, President of the League of Nations Opium Board said, "He is the greatest living authority on the world narcotic traffic." Congressman Carroll Reece in the Congressional Record for December 2, 1943 said, "The Sunday Star of November 28, 1943 hailed the British and Dutch announcements as a diplomatic triumph for the United States. Honorable Harry J. Anslinger is largely responsible for this diplomatic triumph." Congressman Gordon Canfield's comment in the Congressional Record was, "He is not only one of America's great administrators but one of the finest administrators in the world."

But not only has our Commissioner been successful in his diplomatic efforts to subdue illicit international traffic in narcotic drugs, he also during all of these years has had the additional stupendous task of supervising and enforcing the policing of illicit traffic in our own United States, of breaking up the smuggling of opium, and of caring for and rehabilitating the unfortunate addicts. As a measure of his success in this work, it is significant that whereas in the First World War the Army rejected 1 person for drug addiction out of every 1500 examined; during the Second World War there was only 1 rejected out of every 10,000.

Although all of these activities which I have enumerated have been concerned with the evil side of narcotics, our Commissioner has been equally concerned that their legitimate use shall not have been curtailed. During World War II, when opium was classified as a critically needed item both for military and civilian use, his foresight enabled our government to fill the vaults of the Treasury Building in Washington, then recently vacated by removal of our gold reserves to Fort Knox, with invaluable opium. This resulted in our having a supply of narcotic drugs throughout the war period not only sufficient for civilian and armed-forces needs, but for the needs of our Allies as well. For this act, Representative John J. Cochran stated in Congress, "Mr. Anslinger deserves a medal of honor for his advanced thought."

I wish I might have had the time to turn back to Mr. Anslinger's pre-commissioner days, to tell you more about his equally important work in the diplomatic service of his country,—how for example, he was the first to warn the British Intelligence Service, of the Russian

Third Internationale plans to spread revolution throughout the world, and how this startling report was published in British newspapers to awaken the public. And how during World War I, Mr. Anslinger was appointed Attaché of the American Legation at The Hague to obtain information behind the German lines. Under great secrecy he was dispatched to England and there reported to the British Admiralty, who finally notified him they would have him escorted across the North Sea with a fleet of fourteen destroyers because of the submarine danger. On the night the British Admiralty told him to pack his bags and get ready for the voyage, he was about to leave the hotel room when he found a letter under his door. Upon opening it he found a message which read: "Dear Mr. Anslinger: The Imperial German Government welcomes you to the great world conflict."

And now, for the first time, I am able to tell you about an achievement of his during the first World War which had it been known at the time would have been sensational. Before the Armistice, he was instructed to attempt to accomplish personal communication with the entourage of Kaiser Wilhelm II in order to verify certain plans of the German Empire which had been reported from a neutral country. By some adroit means hitherto undisclosed, and which must remain so, he managed to travel with the Kaiser's entourage and remain with the staff until the Armistice, being able to act as an intermediary for exchange of views between his Government and the Kaiser's staff. He could reveal the secret of the fake armistice of November 7, 1918, but I doubt if we could pry it out of him.

In conclusion, I like the words of Senator Paul H. Douglas in the *American Magazine* for October, 1951, in which he recommended, "public praise for Commissioner Anslinger for the fine, devoted and tireless job he is performing—*quietly*." I like that word "quietly," for it so aptly describes those characteristics of modesty and friendly comradeship that so endear our honored guest to his very many local personal friends in the Philadelphia Drug Exchange, and why we look forward each Spring and Fall to have him join us in our semi-annual outings. We all know that he swings a mean golf stick, but at the great risk of committing an unfortunate anti-climax, may I tell you a little story of his prowess in football?

It seems that during his high school days in Altoona he played half-back on the football team. The manager made the unfortunate error of scheduling a game with the Carlisle Indian freshmen. The score was 40-0 in favor of Carlisle. The Altoona papers in describing

the game remarked: "The most brilliant run of the day for the Altoona High School team was made by half-back Harry Anslinger who lost eight yards on the play".

And now I come to the most important part of our program. Mr. Anslinger, it gives me great pleasure, on behalf of the Philadelphia Drug Exchange to present to you this citation which reads:—

PHILADELPHIA DRUG EXCHANGE

PROCTER MEDAL

in memory of

WILLIAM PROCTER, JR.

(1817-1874)

Father of American Pharmacy

and

Pioneer in Drug Research

awarded to

HARRY J. ANSLINGER, LL.B.

for distinguished services to the pharmaceutic arts and in the interest of the public welfare as Administrator, Author, Diplomat, Lecturer and Representative of the United States of America at many international conferences:

and specifically for his eminent leadership in, and his unselfish devotion to, the world wide control of traffic in Narcotic drugs, thus enhancing the prestige of the American Drug Industry and contributing greatly to the physicial, mental and moral welfare of all humanity;

and for his many contributions to general publications and specialized magazines in criminology and medicine.

These accomplishments, which have served to merit this highly appropriate recognition, have been consummated through his work as:

Appointee to Diplomatic Posts in the Netherlands, Germany, Venezuela and the Bahamas;

Consultant and Advisor of many Governments on Narcotic Control;

Chief of the Division of Foreign Control, U. S. Treasury Department;

United States Delegate, League of Nations International Conference for Suppression of Illicit Traffic in Narcotic Drugs;
Delegate of the United States of America to International Conferences in London, Paris, Antwerp, Ottawa and Geneva;
United States Representative on the United Nations Commission on Narcotic Drugs;
Member of the Efficiency Board, Ordnance Division, War Department;
Chairman, Advisory Committee on International Co-operation in Criminal Law Administration, American Bar Association;
United States Commissioner of Narcotics in the Treasury's Bureau of Narcotics since its founding in 1930.

In Testimony Whereof, we have hereunto set our hands, this Fifth day of February, A. D., Nineteen hundred and fifty-three.

(Signed) A. B. Collins
President
J. Mervin Rosenberger
Secretary
R. G. Anderson
Chairman, Award Committee

And with it goes this gold medal, with all of our admiration, respect and affection.

# MODERN MEDICINALS IN REVIEW

By Robert E. Abrams

THE year 1952 was another banner year in the pharmaceutical industry, producing a large number of specific therapeutic agents. The trend toward specific therapeutic agents is continuing, although an increasing number of combinations and duplicate products are being placed on the market. There follows a review of a number of the major therapeutic advances of the year 1952.

## Adrenergic Blocking Agents

*Regitine*

This new potent adrenolytic agent is recommended for the diagnosis of pheochromocytoma, for peripheral vascular disorders, and for hypertensive crises. Pheochromocytoma has been shown to occur more frequently than once believed and the tumor, which in most instances arises from the adrenal medulla and discharges excessive amounts of epinephrine into the blood stream, may be the causative agent of paroxysmal hypertension. Regitine is useful also in the medical management of patients with pheochromocytoma besides in its diagnosis. It will prevent paroxysmal attacks in the preoperative preparation of the patient and during the actual removal of the tumor.

The drug, having a marked adrenolytic and sympatholytic effect, is a valuable adjunct in the treatment of certain peripheral vascular diseases including Raynaud's disease, arteriosclerosis obliterans, Buerger's disease, diabetic arteriosclerosis and ulcers of the extremities.

Regitine is available from Ciba Pharmaceutical Products Inc. in ampuls for intramuscular or intravenous use, each ampul containing 5 mg. of Regitine methanesulfonate in lyophilized form. It is also supplied in 50 mg. scored tablets for oral use.

*Dibenzyline*

A derivative of Dibenamine, Dibenzyline has been shown to be somewhat less toxic than the parent compound. It has the property of blocking the basic action of epinephrine, especially its constricting effect on the peripheral vascular system. Dibenzyline is effective

orally and is relatively safe, but nausea and vomiting are possible side reactions. Its action is specifically against epinephrine as it does not affect blood pressure in itself. This drug is currently under investigation by Smith, Kline and French Laboratories and should be released early in the spring.

## Amebicides

*Milibis*

A new amebicide which has changed the therapeutic outlook in the treatment of intestinal amebiasis, Milibis is a bismuth glycolarsanilate. It is claimed to be over 90 per cent effective in the treatment of amebiasis and to possess extremely low toxicity. The product is available in 25 mg. and 50 mg. tablets.

It is also effective in the treatment of trichomonas vaginitis, monilial vaginitis and bacterial vaginitis. The drug is available in glycerogelatin vaginal suppositories.

Winthrop-Stearns also markets a combination of Milibis and Aralen recommended for the treatment of amebiasis which supplements the effect of Milibis acting on the cyst forms in the liver and brain tissues. Each tablet contains Milibis 250 mg. and Aralen diphosphate 75 mg.

## Analgesics

*Acetyl Para-aminophenol*

Although not new, this compound has been re-released after being withdrawn from the market following reports of granulocytopenia possibly caused by the drug. However, a careful investigation failed to reveal such dangers and the drug has again been made available. Acetyl-*p*-aminophenol is a rapidly acting analgesic and antipyretic compound which is a metabolite of acetanilid and offers the advantages of acetanilid without the danger of the formation of sulf-hemaglobin.

A combination of the drug with aspirin and caffeine is available from E. R. Squibb and Sons under the title of Trigesic as well as Trigesic with Codeine tablets and is recommended in neuralgia, musculoskeletal pain, and for severe pain of nervous origin.

Acetyl-*p*-aminophenol is also marketed by the Ames Co. under the name of Apamide and a combination of it with acetylcarbromal is available as Apromal.

*Cobroxin*

A new potent analgesic substance derived from cobra venom, Cobroxin is available in 1 cc. ampuls from Hynson, Westcott, Dunning Inc. It is recommended to relieve intractable pain, particularly in patients with inoperable malignancy. It eliminates or reduces the need for narcotics and is administered subcutaneously or intramuscularly when the severity of pain reaches a point requiring codeine.

*Fiorinal*

A combination of isobutyl-allyl-barbituric acid, 50 mg.; Caffeine, 40 mg.; aspirin, 200 mg., and acetophenetidin 130 mg., this product is offered by Sandoz Pharmaceuticals for the treatment of tension headaches, headaches due to sustained muscle contraction, sinusitis, and dental pain.

## Anesthetics

*Efocaine*

Offering a new approach to local anesthesia, Efocaine is a non-oily repository solution of procaine and butylaminobenzoate. Recommended for use in the prolonged management of pain, the product is slowly absorbed from the site of injection and assures safe and continuous local anesthesia over a period of 6 to 12 days or longer.

The product is indicated post-operatively in hemorrhoids and in minor surgery as well as for the relief of pruritus ani and pruritus vulvae. It is available in multiple dose vials from E. Fougera & Company.

*Trilene*

This is highly purified trichlorethylene. Trilene is offered for inhalation analgesia and can be self-administered with relative safety. It provides analgesia without loss of consciousness or momentary unconsciousness. The Duke University Inhaler is recommended for its administration.

It is employed as an analgesic adjunct to various anesthetics, in obstetrics, and surgery and also to provide relief from severe intractable pain in carcinoma, trigeminal neuralgia, migraine and dysmenorrhea.

The product is manufactured by Ayerst, McKenna and Harrison and is available in 300 cc. containers and 6 cc. ampuls.

## Antacids

*Trimucolan*

A new mucin-antacid preparation for treating peptic ulcer, Trimucolan combines 0.16 Gm. of gastric mucin; 0.25 Gm. of dried aluminum hydroxide gel and magnesium trisilicate and is relatively effective in the antacid approach to peptic ulcer. The product is available in tablets and produced by Winthrop-Stearns.

## Antiarthritics

*Benemid*

A benzoic acid derivative, *p*-(di-n-propylsulfamyl) benzoic acid or Benemid, is an effective uricosuric agent recommended in gout and chronic gouty arthritis. It may be administered alone or it can be given with full doses of colchicine in treating an acute attack of gout. Benemid will materially increase the excretion of uric acid by the kidney. It is available from Sharp and Dohme in 0.5 Gm. tablets.

*Butazolidin*

A non-steroid, Butazolidin is a pyrazolone derivative (phenylbutazone) which has been shown to be orally effective in the treatment of rheumatoid arthritis, inflammatory and musculoskeletal diseases and particularly in gout. It possesses an analgesic, antipyretic and anti-inflammatory action and in gout is more effective than salicylates of colchicine. Although originally claimed to be non-toxic, the product has produced serious side reactions including hematemesis, sodium retention and agranulocytosis; it should never be used in patients suffering from peptic ulcer. It is manufactured by Geigy Co. and available in yellow coated tablets of 200 mg. and red coated tablets of 400 mg.

*Cortisone and Hydrocortisone*

A number of companies have placed cortisone preparations on the market over the past year. Included among these are the Schering Corporation (Cortogen) and the Upjohn Company (Cortisone). In addition Merck & Co. has made available Hydrocortone (also known as Kendall's Compound F or Reichstein's Substance M). Hydrocortisone acetate differs from cortisone acetate in having an alcohol group at the eleventh position in the steroid nucleus rather than a ketone group.

Extensive investigations seem to reveal that hydrocortisone acetate may be even more active than cortisone acetate in the treatment of rheumatoid arthritis and related conditions. The product is presently available in both injection and tablet form. The injection is a saline suspension of 25 mg. of hydrocortisone acetate and is recommended for local injection into the articular cavity of a rheumatoid or osteoarthritic joint. It is effective when only one or two joints are affected and its effect is only local, producing a prompt and prolonged relief from pain, stiffness, tenderness and swelling without producing a systemic action.

The tablets of hydrocortisone acetate, available only on clinical trial, seem to be more effective than tablets of hydrocortisone, cortisone and cortisone acetate.

## Antibiotics

*Chloromycetin*

One of the significant developments during the past year in the antibiotic classification was the furor caused by various reports of serious blood dyscrasias caused by the broad spectrum antibiotic Chloromycetin. Several reports published in the J.A.M.A. placed the responsibility of a number of deaths on this drug which resulted in a marked decline in its use. However, latest reports indicate that the earlier panic was somewhat unfounded and that Chloromycetin when used under adequate supervision is not dangerous. The drug, to be certain, in 1953 will again take its place alongside the other wide spectrum antibiotics in the treatment of many diseases.

A number of newer dosage forms have been released over the past year in this broad spectrum field. In the case of Aureomycin, 1952 has brought as a calcium oral suspension, calcium syrup, a nasal solution, suppositories and a vaginal powder. Terramycin has also been released in tablets, dental cones and paste, nasal, oral suspension, otic solution and vaginal suppositories.

*Bicillin*

A dipenicillin salt (N,N'-dibenzylethylenediamine dipenicillin-G) Bicillin yields much higher blood levels than procaine penicillin preparations. The combination is not very soluble and therefore is quite stable and tasteless in aqueous suspension. The product, manufactured by Wyeth, Inc., is available in a flavored suspension for oral use

which is stable up to 18 months, in an aqueous suspension for parenteral use, as Bicillin L-A, and as a long acting tablet which can be administered every 12 hours and which produces adequate penicillin blood levels.

*Neo-Penil*

First reported in Denmark and studied extensively in this country, Neo-Penil has been released by Smith, Kline and French Laboratories for those infections which respond to repository penicillin. The product is the hydriodide of the β-diethylaminoethyl ester of penicillin G. Its advantage lies in the fact that it concentrates in certain tissues such as lung, lymph nodes, spinal fluid, umbilical cord blood and other areas. It is available in vials and is administered intramuscularly.

*Erythromycin*

Marketed presently by two companies, Abbott Laboratories (Erythrocin) and Eli Lilly & Co. (Ilotycin), this new antibiotic was isolated from a culture of an organism obtained from a soil sample taken from the Philippine Islands. It is produced by a strain of *Streptomyces erythreus* and is effective against gram-positive organisms and some of the more important gram-negative organisms. It is also claimed to be effective against organisms which have become resistant to penicillin.

This antibiotic after administration has been found in the blood, urine, feces, cerebrospinal fluid. It is concentrated in the liver and excreted in quantity in the bile. It diffuses into the placental circulation, into ascitic fluid and into pleural exudates.

The antibiotic is relatively non-toxic and free from side reactions. It is available in enterically coated tablets of 100 mg. each.

*Neomycin*

The use of neomycin topically is well established and a number of products have been made available employing the antibiotic for the treatment of pyogenic skin infections due to gram-positive and gram-negative organisms. It is recommended in the treatment of many external infections including otitis media.

In addition to the topical forms The Upjohn Co. has made available neomycin tablets containing 0.5 Gm. of the sulfate which is equiv-

alent to 0.35 Gm. of the base. Since it is not absorbed, it is recommended as an antibacterial agent in preparing patients for gastrointestinal surgery. Commercial Solvents Corp. also has available *Neobacin* tablets which are recommended for similar use. These contain a combination of Neomycin and Bacitracin.

The topical preparations include the product *Neosone* by The Upjohn Co. which is a combination of neomycin and cortisone and indicated in ophthalmic infections. *Spectrocin* by E. R. Squibb & Sons which combines neomycin and gramicidin in a topical ointment, an ophthalmic ointment and in troche form; and combinations with Bacitracin as in the product *Bacimycin* by Walker Laboratories and *Neobacin* Ointment by Commercial Solvents Corp.

*Newer Antibiotics*

*Achromycin* (Lederle Laboratories) has been obtained from the soil from an old Wisconsin Indian burial mound. This chalk white mold produces an antibiotic effective against the causative agent of African Sleeping Sickness.

*Cardicin; Rhodocidin; Thioaurin* (Sharp and Dohme, Inc.). These are presently under investigation with Cardicin reported to be effective against certain yeasts, molds and bacteriophages while the others are effective against some gram-positive and gram-negative organisms.

*Magnamycin* (Chas. Pfizer & Co.) is a substance which may prove effective against bacteria which are resistant to penicillin and streptomycin. Studies indicate that it does not show cross resistance with other antibiotics in general use. It has been found to destroy most gram-positive bacteria but is ineffective against gram-negative bacteria.

*Madronin:* From the leaves of the Pacific Madrona tree a water soluble antibacterial agent can be extracted. The principle is active against the gram-positive organisms but not against the gram-negatives.

*Vivicil* (Schenley Laboratries). This substance is being investigated and early reports indicate it is effective against various pathogenic fungus diseases.

## Anticoagulants

*Hedulin*

A new oral anticoagulant 2-phenylindane-1,3-dione, Hedulin is not a coumarin derivative. It is useful in thromboembolic diseases including thrombophlebitis, pulmonary embolism, phlebothrombosis and coronary, aortic and cerebral thrombosis.

The drug will rapidly lower the prothrombin level in 18 to 24 hours and prothrombic concentrations return to their initial value in 24 to 48 hours. Rapid elimination and dosage procedures minimizes the danger of hemhorrhage and Hedulin is effective in the prophylaxis and treatment of intravascular clotting. It is available from Walker Laboratories, in tablets of 50 mg.

## Anticonvulsants

*Gemonil*

A barbituric acid derivative (5,5-diethyl-1-methylbarbituric acid) Gemonil has been shown to be effective in treating grand mal, petit mal, myoclonic epilepsy and mixed seizures. It is especially effective in the control of myoclonic seizures and in conditions where the symptoms are due to organic brain damage.

It may be used in conjunction with Tridione, Paradione, Phenurone and the hydantoins. The product is supplied in 0.1 Gm. tablets by Abbott Laboratories.

*Hibicon*

Chloroethylphenamide, a new antiepileptic compound has just been released by Lederle Laboratories. It is administered oraliy and has shown best results against grand mal. Clinical tests indicate that the drug is effective in some cases where other established anticonvulsants have failed. Based on a chemical structure never before used in epilepsy, the drug is apparently well tolerated.

*Themisone*

Not yet available this new anticonvulsant agent has been developed by Mallinckrodt Chemical Works. An aromatic hydroxyamide derivative, the compound has been reported successful in the treatment of grand mal and psychomotor seizures. The drug is not effective against petit mal but is effective where both grand mal and petit mal are present in the same patient.

## Anti-Infectives

*Furadantin*

The first nitrofuran compound developed for systemic use on humans, this antibacterial agent is now undergoing clinical trial. The drug is being tested in the treatment of *B. proteus* infections of the urinary tract, cystitis and pyelonephritis. The drug was found to be safe and effective in giving relief from all urinary symptoms without any toxic effects. It has been developed by Eaton Laboratories.

*Elkosin*

This relatively new sulfonamide, a homologue of sulfamethazine, is an extremely effective antibacterial agent in treating urinary tract infections due to both gram-positive and gram-negative organisms.

It has the advantage of being soluble in neutral and slightly acid media and does not require concurrent administration of alkali. Acetylation is low, about 10 per cent, and thus high blood levels may be obtained with smaller dosage. It is available from Ciba Pharmaceutical Products Inc. in tablets and in syrup form.

## Antimalarials

*Daraprim*

A new antimalarial compound which is extremely potent, Daraprim is about to be released by Burroughs and Wellcome & Co. A potent single treatment for malaria, the drug is relatively inexpensive and offers hope for the effective control of malaria.

## Antihistamines

Injectable antihistamines have proved valuable in preventing allergic reactions to pollen extracts, penicillin, blood transfusions and similar treatments over the past year and their inclusion routinely has been recommended.

*Co-Pyronil*

A combination of two antihistamines, Co-Pyronil exhibits a more prolonged action than other compounds. The new antihistamine Pyronil has a slow onset of action and so it was combined with faster acting. Thenylpyramine and the sympathomimetic, Cyclopentamine resulting in Co-Pyronil which gives prompt action and prolonged re-

lief. Chemical reports indicate that results are impressive in a large number of cases while side effects are usually negligible. The products is available from Eli Lilly & Co. in capsule form.

*A-P-Cillin and Bristapen*

Two combinations containing A.P.C., penicillin and the antihistamine phenyltoloxamine, are offered for the management of acute upper respiratory infections including the common cold. While the rationale of this combination is questionable, these products are probably forerunners of a number of similar ones that will be made available. The former product is available from White Laboratories while the latter is manufactured by Bristol Laboratories.

## Antihypertensives

*Hydergine*

A combination of the hydrogenated alkaloids of the ergotoxine series from ergot, Hydergine contains 0.1 mg. each of dihydroergocornine, dihydroergokryptine and dihydroergocrystine as methanesulfonates. Originally investigated for the treatment of migraine, it was discovered that the compounds had a definite sympatholytic action and were effective in reducing blood pressure. One of the advantages of the compound was the fact that instead of producing a tachycardia as do many hypotensive agents it produced a bradycardia which also aids in the reduction of blood pressure. The product is produced by Sandoz Pharmaceuticals and is only effective by injection.

*Hexamethonium*

C6, as it is commonly known, is a powerful ganglionic blocking agent which is capable of producing a fairly long acting peripheral vasodilation. A great deal of publicity was given this drug and combinations of it with Apresoline in the lay press, as a "wonder drug" for hypertension. Although useful, it is potentially dangerous and adequate precautions should accompany its use. It is recommended in the treatment of hypertension and acute peripheral vascular disorders associated with neurogenic vasospasms. In most cases of benign essential arterial hypertension it will markedly reduce the blood pressure and has also been reported to be helpful in malignant hypertension.

The product is marketed as the chloride by Chilcott Laboratories under the title of *Methium* and available in 125 mg. and 250 mg. tablets; by Burroughs and Wellcome & Co. as *Hexameton* in 250 mg. and 500 mg. tablets; and as *Esomid* by Ciba Pharmaceutical Products Inc. who offer a 250 mg. tablet and a Syrup containing 250 mg. per teaspoonful. It is also available as the bromide for parenteral use under the title of *Bistrium Bromide* from E. R. Squibb & Sons.

*Apresoline*

Hydralazine hydrochloride (1-hydrazinophthalazine hydrochloride) is a new hypotensive agent which acts in a unique manner. It increases renal blood flow through a marked vasodilatation of the renal arteries and is claimed to have an inhibitory action on the hypertensins, including angiotonin and other endogenous factors, which have been described as causative agents in hypertension.

The drug will produce a gradual and sustained hypotension with no abrupt fall. A dangerous hypotension may be produced by excess dosage. It is wise that its use be carefully controlled at first with frequent checks made on blood pressure. A number of patients will develop tolerance to the drug and if this occurs it should be discontinued for about a week when it can then be reinstituted. Its combined use with Methium has been suggested thus approaching the treatment from two different directions, delaying the development of tolerance as well as partially reducing the side reactions by the use of smaller dosage.

Certain side effects may be produced by Apresoline but on continued use these usually disappear. The drug should be used with extreme caution in patients with diseases of the coronary artery, advanced renal damage, and cerebral vascular damage. It is available from Ciba Pharmaceutical Products Inc. in 10 mg., 25 mg. and 50 mg. tablets.

*Veratrum*

This drug has been a matter of controversy for hundreds of years but veratrum has been back in the medical picture the last several years. A number of antihypertensive products have included veratrum in their combinations. Veratrum does have a sympatholytic action and has been helpful in the treatment of hypertension. Several products have appeared on the market. A new approach was the

release of *Veroloid* Intravenous Solution by Riker Laboratories. Of definite advantage, the product requires a great deal of care in its use and should be employed only in emergency.

Another for the control of hypertension is the E. R. Squibb product *Vergitryl* which is the ester alkaloid fraction of *Veratrum viride,* standardized by the carotid sinus pressor reflex method. The dosage with this product must be carefully regulated since the margin between the emetic dose and effective dose is narrow and in certain cases non-existent.

Sandoz Pharmaceuticals have isolated a new alkaloid from veratrum album, known as *Veralbidine* it has shown promise and may be available during the next year.

## Antiseptics

*Actamer*

Monsanto Chemicals has developed a new synthetic bacteriostatic agent effective against gram-positive organisms. It has been shown to be useful in the presence of soap and other detergents and can be employed in soaps, etc., where control of skin bacteria is indicated. A chlorophenol derivative 2, 2' thiobis (4,6-dichlorophenol) the product is claimed to be effective against gram-positive cocci, frequently the causative agent of boils, carbuncles and other skin infections. It may be used in pre-surgical scrubbings, in shampoos, shaving creams and skin lotions. Preliminary tests indicate a low incidence of sensitization.

## Antispasmodics

*Antrenyl Bromide*

This new potent anticholinergic compound is chemically diethyl (2-hydroxyethyl) methyl-ammonium bromide phenyl-cyclohexane-glycolate. It is recommended for the medical management of peptic ulcer and spasms of the gastrointestinal tract. It materially reduces gastric hypermotility and produces a significant reduction in gastric secretion.

It is claimed to produce less side reactions than atropine but dryness of the mouth, blurring of the vision, urinary retention and constipation may often be noticed.

It is contraindicated in the presence of glaucoma, pyloric obstruction or prostatic hypertrophy. It is effective in much smaller

dosage than the two similar products available (Banthine, Prantal). It is marketed by Ciba Pharmaceutical Products Inc. in 5 mg. tablets and in a syrup containing 5 mg. per teaspoonful.

*Prantal Repeat Action*

This is a new dosage form of the anticholinergic agent Prantal. It is a 100 mg. tablet made available by the Schering Corp. and is claimed to eliminate nocturnal hypersecretion if taken at bedtime. The tablet is designed so that 50 mg. is contained in the upper coatings of the tablet and is released quite rapidly while 50 mg. is contained in an enteric coated portion which is later released.

*Trihexyphenidyl*

Trihexyphenidyl hydrochloride is recommended for the treatment of Parkinsonism. It is said to act without side effects in most cases, to promptly relax rigidity in all types of Parkinsonism and sometimes obliterate the tremor.

It has no ill effects on blood pressure, respiration, erythrocyte and leukocyte count, liver, kidneys, and sugar metabolism and will not precipitate glaucoma. It is useful in Parkinsonism, whether postencephalitic, idiopathic or arteriosclerotic in origin. The drug is available in 2 mg. tablets from Winthrop-Stearns as Pipanol Hydrochloride. The same substance is available from Lederle Laboratories as Artane.

## Antitubercular Agents

*Isoniazid*

The premature release of results obtained with the use of isonicotinic acid hydrazide raised the hopes of many sufferers of tuberculosis and set up a public clamor probably unprecedented in pharmaceutical history.

Preliminary results obtained with patients previously believed incurable were encouraging. Recovery was quite rapid with increase in weight, the clearing of the sputum and reduction in temperature evident. The healing of lesions, however, was not rapid and frequently did not occur. Although the progress of the disease is halted and temperature returns to normal the emergence of drug resistant forms of *M. tuberculosis* takes place.

Recent reports indicate that a combination of Isoniazid and Streptomycin appears to be superior to P.A.S. and Streptomycin and

probably a combination of all three therapeutic agents may become the treatment of choice in tuberculosis to eliminate the emergence of resistant strains. The long range studies which are necessary to prove effectiveness in the treatment of tuberculosis have not yet appeared but 1953 should bring forth much more definite information on the status of this new drug.

With the clamor produced by the news of this agent we witnessed a great influx of trademarked products, all containing the drug in tablet form. Among these are:—*Armazide* (Armour Laboratories); *Cotinazin* (Chas. Pfizer & Co.); *Dinacrin* (Winthrop-Stearns); *Ditubin* (Schering Corp.); *I. N. H.* (Eli Lilly & Co.); *Isolyn* (Abbott Laboratories); *Isoniazid* (Upjohn Co.); *Niconyl* (Parke Davis & Co.); *Rimifon* (Hoffman-La Roche); *Nydrazid* (E. R. Squibb & Sons); *Pyricidin* (Nepera Chemical Co.); *Tisin* (Casimir Funk); *Tyvid* (Wm. S. Merrell Co.).

An isopropyl derivative of isoniazid, known as iproniazid, is produced by Hoffman-La Roche under the title of Marsalid. E. R. Squibb & Sons also have available a *Nydrazid Injection* (isoniazid) which is suggested in cases where oral administration is not feasible.

*Aldinamide*

Still under study is the product pyrazinamide (Aldinamide, Lederle Laboratories) which is closely related to isonicotinic acid hydrazid. It has shown effectiveness against the usual strains of tubercule bacilli as well as against strains which have become resistant to streptomycin.

## Antitussives

*Toryn*

Caramiphen ethanedisulfonate (Toryn—Smith, Kline and French Laboratories) is a new non-narcotic compound for cough control. It acts specifically on the cough reflex centers and is recommended for all types of coughs. It is reported to have little or no effect on respiration and does not exhibit the various side reactions seen with codeine whose action it resembles. It is available in both tablet and syrup form.

## Cancer and Leukemia

Although 1952 was a year of unprecedented effort in the field of cancer research we still have a long way to go in understanding this

dread disease and developing therapeutic agents to combat it. The use of nitrogen mustard ($HN_2$) has shown some promise and its effects and limitations are now under extensive study.

*Aminopterin*

A folic acid antagonist Aminopterin (4-amino-pteroylglutamic acid) is available for the treatment of children with acute leukemia. It is of little value in treating leukemia in adults. The drug has potential toxic effects and may cause severe depression of all blood cellular elements and it is extremely important that the physician utilize extreme care in using the drug.

The product is available from Lederle Laboratories in tablets of 0.5 mg.

*Krebiozen*

A great deal of controversy developed concerning this drug which was claimed by a Czecloslovakian physician to have cancer curing properties.

However, after extensive controlled tests the American Medical Association published a report that it was impossible to show any effect whatever in the treatment of cancer by the use of this drug.

## Diagnostic Aids

*Telepaque*

This is a new cholecystographic medium which produces superior visualization with a much smaller dosage than any cholecystographic agent available. The compound exhibits a minimum of side reactions. Its chemical formula is 3(3-amino-2,4,6-triiodophenyl)-2-ethylpropanoic acid and it contains 66.68% iodine by weight. It is available from Winthrop-Stearns in packets of six tablets.

*Terodax*

This is a product very similar to Telepaque, alpha ethyl-beta (2,4,6 triiodo 3 hydroxyphenyl) propanoic acid and it is now being studied by Schering Corp. Given the name Terodax, it produces a much clearer delineation of the gall bladder than does iodoalphionic acid. The drug is orally effective and can be administered in tablet form.

## Diuretics

*Cumertilin Sodium*

A combination of sodium mercumallylate and theophylline the product differs somewhat in structure from other mercurial diuretics. However, its effect is very similar to that produced by other mercury and theophylline compounds. Its injection causes local irritation similar to that produced by other mercurial diuretics. Although it is recommended both for intramuscular and intravenous use the intramuscular route is to be preferred. The solution in 1 and 2 cc. ampuls is marketed by Endo Products Inc.

*Neohydrin*

A true advance in mercurial diuretics, Neohydrin is orally effective and is claimed by its manufacturer to produce a result comparable to a mercurial injection. Chemically it is 3-chloromercuri-2-methoxy-propylurea. The recommended dosage is one 18.3 mg. tablet daily which can be increased if the response is not favorable. It exhibits many of the usual side reactions produced by the mercurials. The product is manufactured by Lakeside Laboratories, Inc.

## Endocrines

The products cortisone and hydrocortisine have been mentioned under antiarthritics. The year 1952, with regard to endocrine products, was more of a developmental era rather than a year of discovery. A.C.T.H. and cortisone were studied extensively and the uses and limitations were explored. A number of new dosage forms appeared and probably one of the most important was *H. P. Acthar Gel* (Armour Laboratories); a highly purified A.C.T.H. in a long acting repository vehicle. It can be used both subcutaneously and intramuscularly and is stable at room temperature.

## Hormones

*Sulestrex Piperazine*

A new form of conjugated estrogen this product is piperazine estrone sulfate. It has the advantage of not imparting an odor to the breath or perspiration and does not produce an unpleasant taste. The product is supplied by Abbott Laboratories both plain and combined with methyl testosterone. Buccal or sublingual tablets are available.

The combination of methyl testosterone with various estrogens was shown to have certain decided advantages and a number of popular estrogenic products were released in combination with testosterone.

*Tace*

Known as chlorotrianisene or tri-*p*-anisyl-chloroethylene it is a new synthetic estrogen, particularly recommended in the treatment of prostatic cancer. It is chemically similar to other synthetic estrogens as diethylstilbestrol and hexestrol, however, it has two methoxyphenyl groups instead of two hydroxyphenyl groups and the two ethyl groups are replaced by a methoxyphenyl and a chlorine group. Unlike other synthetic estrogens in test animals, Tace produces a minimal enlargement of the adrenal gland and no enlargement of the pituitary gland.

The side effects are much reduced with this drug and nausea and vomiting are seldom produced. In one series of cases studied all patients suffering from prostatic carcinoma showed definite regression or disappearance of physical evidence of cancer of the prostate. The drug is indicated in cases where it is inadvisable to employ diethylstilbestrol or where the gastric irritation produced by other synthetic estrogens is a factor. The product is orally effective and produced by the Wm. S. Merrel Company.

*Vallestril*

The newest of the synthetic estrogens is Vallestril, 3-(6-methoxy-2-naphthyl)-2,2-dimethylentanoic acid. It is recommended for the relief of the symptoms of artificial or natural menopause; postmenopausal osteoporosis and vaginitis; prostatic cancer and suppression of ovulation and lactation.

The product is relatively free from the usual side effects and produces a much lower incidence of withdrawal bleeding. Nausea and edema are also lessened. It is available in 3 mg. tablets and is manufactured by G. D. Searle Co.

## Motion Sickness

*Apolamine*

This is a combination of Luminal, atropine sulfate, scopolamine hydrobromide, benzocaine, riboflavin, pyridoxine hydrochloride and

nicotinamide. Apolamine is suggested as an antiemetic in a number of ailments. It is claimed to control nausea and vomiting in pregnancy, motion sickness, alcoholic gastritis, nonspecific vomiting, anesthesia and radiation sickness and vomiting due to pain-relieving drugs. It is available in tablet form from Winthrop-Stearns.

*Benadryl with Hyoscine*

This product by Parke Davis & Co. combines the antihistaminic action of diphenhydramine with the parasympatholytic action of scopolamine hydrobromide. It is recommended for the treatment of motion sickness and similar conditions.

## Muscle Relaxants

*Anectine*

Succinylcholine chloride is a skeletal muscle relaxant for use in anesthesia where muscle relaxation is desired. It is a helpful adjunct in anesthesia and has the advantage over the curare compounds in being relatively short acting. This shorter duration of action greatly reduces the hazard of respiratory collapse which may occur when curare or curariform drugs are used. Marketed by Burroughs and Wellcome, the product is available in 10 cc. vials containing 20 mg. per cc.

## Poliomyelitis

Several encouraging advances in the treatment of poliomyelitis were made in 1952. First under the auspices of the National Foundation for Infantile Paralysis extensive tests were made using gamma globulin and the results point to the possibility that this substance will prove helpful in protecting against polio or reducing the severity of the condition. In these tests a single injection was effective in protecting over 27,000 children against polio for a period of five weeks after administration.

Unfortunately the protection produced by gamma globulin is not permanent but this five week or more protection afforded will be helpful in times of epidemics. A distribution problem most likely will develop since there will not be a sufficient quantity to allow for mass immunization. Possibly some fair method of distribution will be devised.

Another encouraging development was the announcement that Dr. Harold Cox and his associates at Lederle Laboratories were successful in obtaining an oral polio vaccine using the chick embryo. This vaccine has been shown to be effective only against the Lansing strain of poliomyelitis. However, this strain is the one most prevalent. This new method of producing the vaccine can raise the supply to an unlimited quantity but its effectiveness has yet to be clinically tested.

At Johns Hopkins a vaccine which is effective against all three strains of poliomyelitis has been developed. However, the product had to be grown on the spinal cord of monkeys the usual growing media of many vaccines. This nevertheless indicates that there is a most definite hope that some suitable method will be devised to protect children against this greatly feared disease.

## Sympathomimetic

*Aramine*

A new nasal decongestant, metaraminal bitartrate, is extremely effective in relieving the nasal congestion accompanying coryza, rhinitis, sinusitis and nasopharyngitis. There is some danger involved since it is a powerful sympathomimetic. Tremor, palpitation, tachycardia or insomnia may be produced. It is marketed by Sharp and Dohme packaged with an accompanying dispenser known as the Mijit Atomizer which permits the solution to be used as a spray or drops.

## Vasodilators

*Peritrate*

Pentaerythrityl tetranitrate is a new long acting coronary vasodilator produced by Chilcott Laboratories. It is relatively non-toxic and offers prolonged relief as a prophylactic in the treatment of angina pectoris. It is not recommended to replace nitroglycerin in attacks of angina since its onset of action is much longer. However, it will reduce the frequency of anginal attacks and decrease the nitroglycerin requirement.

## Vitamins

*Covisten and Mediatric*

These products are combinations of multiple vitamins, minerals and hormonal substances recommended in treating the aged where

there is a waning of gonadal function and a diminishing utilization or intake of vitamins and minerals. Covisten (Organon Inc.) contains the anabolic, non-virilizing hormone androstenediol while Mediatric (Ayerst, McKenna and Harrison) contains both conjugated estrogen and androgen in small dosage.

*Panthoderm Cream*

The product is a water-miscible emollient cream containing the analogue of pantothenic acid, Panthenol. It is suggested as a healing aid in diaper rash, prickly heat, rash of measles, chicken pox, for wounds, external ulcers, burns, irritated and chapped skin and other skin conditions.

The product will promote healing and possesses both an antibacterial and antipruritic action. It is available from U. S. Vitamin Corp.

## Miscellaneous

*Betasyamine*

Recently presented as a "wonder" drug by a leading lay publication the drug is a combination of the amino acid betaine and glycocyamine. However, the claims as to the efficacy of the new drug in treating heart disease, rheumatoid arthritis, polio and other conditions were premature and the company, International Minerals and Chemicals, disclaimed any knowledge that information on the new drug was to be published. It will be interesting to see what the future holds in store for this substance.

*Mephyten*

Another new product which is unique Mephyten is a Vitamin $K_1$ emulsion designed for intravenous administration in the treatment of dicoumarol overdosage. The Natural $K_1$ is claimed much more effective for this purpose than menadione. The ampules are available from Merck and Company.

*Nalline*

A product closely related to morphine chemically (N-allylnormorphine hydrochloride) Nalline is a powerful antidote for morphine and other narcotics. It has been shown to offset the respiratory

depression caused by overdoses of morphine and its derivatives within two minutes. Manufactured by Merck and Company it has also been shown to be effective against the synthetic analgesics meperidine and methadon.

*Sodium Dehydrocholate*

The use of sodium dehydrocholate injection has been shown to relieve the symptoms of penicillin sensitivity as well as other forms of serum sickness. A number of cases have proved the value of the substance and it should be the treatment of choice in penicillin reactions.

*Xiphisternal Cartilage*

Sterile Xiphisternal Cartilage from young steers debrided of all adjacent tissue to about 4 x 2 inches and about 1/3 inch thick is available from Armour Laboratories. It is intended as replacement material in reconstructive and plastic surgery. Easily shaped, the product does not cause tissue reactions, is non-absorbed, does not cure or warp, and is fairly simple to employ.

# SELECTED ABSTRACTS

**The Assay of Penicillin by Titration.** Royce, A., Bowler, C., and Sykes, G. *Pharm. J. 169*:305 (1952). The authors describe a method for the assay of penicilloic acid produced from the hydrolysis of penicillin by penicillinase. The acid was titrated with alkali. In the method described the penicillinase was adjusted to a pH of 7.5 using phenol red as the indicator. A portion of this preparation was used as a control. An accurately weighed sample of penicillin was dissolved in water containing phenol red and the pH was adjusted to 7.5. Penicillinase was added and the mixture was allowed to stand at room temperature for 30 minutes. Most of the reactions were found to be completed within 10 minutes but 30 minutes was allowed for assurance. The mixture was then titrated with 0.01 N sodium hydroxide solution until the color matched that of the control. A further period was allowed to elapse to be sure that the reaction had gone to completion and further titration was carried out if necessary. The potency of the penicillin preparation was calculated on the basis that each cc. of 0.01 N sodium hydroxide solution is equivalent to 6023 I. U. of penicillin.

The authors reported that comparison studies showed a mean difference between the titration and cylinder plate assay results of less than 0.1 per cent, and between the titration and iodimetric assay results of 0.9 per cent. The authors also stated that this method of assay had been applied successfully to solutions, oral tablets, penicillin mixtures with insoluble powders, and, with modifications, penicillin in oily bases. Buffer compounds have been found to interfere with the accuracy of the determinations to some degree, but the inaccuracies tend to be minimized when the potency of the preparation is high.

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**Drug Therapy in Elderly Patients.** Salter, W. T. *Geriatrics 7*:317 (1952). The use of drugs in elderly patients requires judicious care so as not to do more harm than good. Elderly patients possess low functional reserves, enfeebled compensatory mechanisms, and possibly an underlying ailment, such as kidney or heart disease, which increases the dangers from the use of drugs.

Declining thyroid hormone production may require replacement therapy in order to protect the cardiovascular apparatus by preventing

hypercholesterolemia. However, overdosage may be fatal. An excess of insulin may cause weakness or even angina in diabetic patients, and an injection of epinephrine for asthma may precipitate a cardiovascular crisis. The detoxification of digitalis is probably less efficiently accomplished with progressing age. Damaged or less efficient kidneys are more readily blocked by sulfonamide crystals.

The number of functioning renal glomeruli decreases with advancing age. Therefore, when drugs have been assimilated they are less readily disposed of and cumulative toxicity is more likely to occur than with a younger person.

It has also been found that the brain of an elderly person is more apt to be disturbed by potent compounds such as digitalis, atropine and, particularly, central nervous system depressants, including anesthetics. A temporary derangement has occurred in many an older person through an attempt to provide a good night's sleep.

The author also pointed out that more vitamins are required by the person advanced in years. The diet should also contain a high level of protein, calcium and iron.

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**The Use of Phthalylsulfacetamide in Anorectal Surgery.** Segal, L. *Am. J. Surg. 84*:684 (1952). In an effort to reduce postoperative pain and morbidity, phthalylsulfacetamide (Thalamyd) was administered pre- and postoperatively to 100 patients with a variety of anorectal conditions for which surgery was performed. The patients were treated with Thalamyd, diet and sitz baths. The Thalamyd was given in a dose of 1 Gm. four times a day for two days prior to surgery and for 2 to 3 weeks postoperatively. The dosage was then reduced to half and continued until complete healing had occurred.

The author reported that the postoperative healing time was reduced by at least 20 per cent when Thalamyd therapy was used. There were no postoperative infections and the patients were more comfortable, more active and required less medication for the relief of pain. These patients also exhibited cleaner wounds, less gas formation, and less odor following surgery. A proctoscopic examination revealed a normal mucosa following Thalamyd therapy. No allergic reactions and no complications of any kind, including diarrhea, followed the use of this sulfonamide. Previous experience with some of the other non-absorbable sulfonamides, aureomycin and terramycin showed the development of diarrhea in many cases. Proctoscopic examination of the latter cases usually revealed a red and ulcerated mucosa.

Thalamyd has been found to be an active bactericidal agent which is absorbed into the intestinal wall but not into the blood stream. It has been found that it is possible to reduce the bacterial count to 10,000 organisms per Gm. of wet feces, which is considered effective sterilization of the gut for surgery.

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**A Sterility Test for Neoarsphenamine and Sulfarsphenamine.** Sykes, G., Royce, A., and Hugo, W. B. *J. Pharm. Pharmacol. 4*:366 (1952). Any substance intended for parenteral administration must be tested for sterility even though it may be toxic or potentially toxic to bacteria. Two general methods are employed in such cases, dilution beyond the concentration providing bacteriostasis or the addition of an inactivating agent. In the case of arsphenamine and sulfarsphenamine the inhibitive concentrations to many of the common bacteria ranges between 1:10,000 and 1:100,000 in nutrient broth. Dilution is, therefore, not practical.

It has been shown that arsenic interferes with some essential enzyme system containing a thiol group. Its action can be counteracted by the addition of compounds containing the thiol group. Heat coagulated muscle was found to provide the thiol groups needed. Therefore, the authors prepared a nutrient broth test media with 0.4 per cent sodium thioglycollate and also the same media with about a 1 cm. layer of heat coagulated muscle added. *Staphylococcus aureus, B coli, B. prodigiosum, B. subtilis,* and *Cl. sporogenes* were used as the test organisms. Very small inoculums of the organisms were added to the two culture media to which had been added 1:100 or 1:200 concentrations of the arsenicals. Daily viable plate counts were made. It was found that the thioglycollate meat broth gave excellent growth with either concentration of the arsenical. A maximum growth curve was attained in about 5 days.

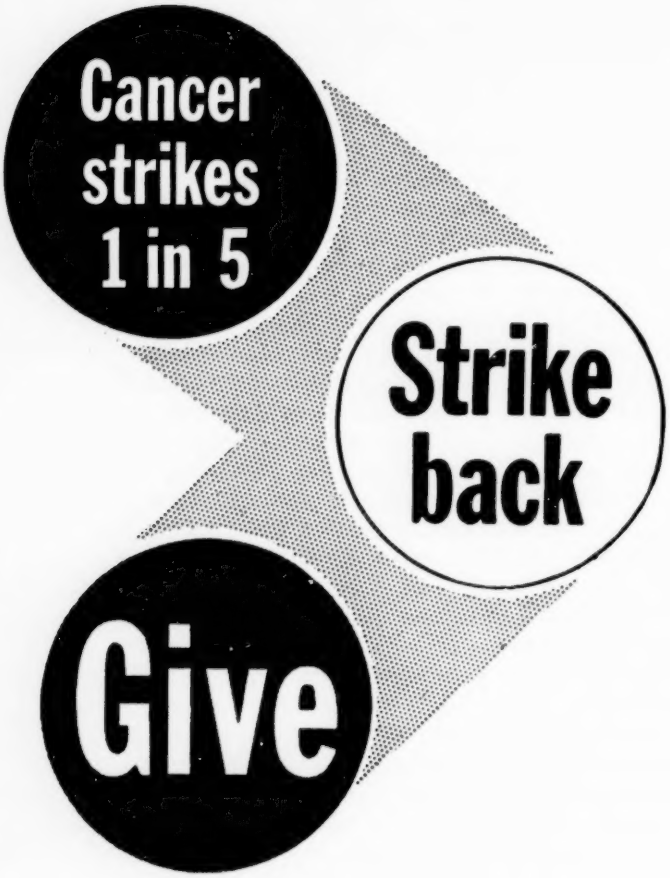
The authors, therefore, suggested a sterility test procedure using a tryptic digest of heart muscle for the basic nutrient broth with the addition of 0.4 per cent sodium thioglycollate and a 1 cm. layer of heat coagulated muscle. The test sample of the arsenical is diluted 1:200 or more. After incumbation at 37 C. for 5 days the medium will become turbid and it is, therefore, necessary to confirm the presence or absence of growth by inoculation of a loopful into a fresh tube of thioglycollate broth.

An addendum by C. E. Coulthard and B. H. Chantrill showed that spores of *Cl. septicum* sealed in ampules of neoarsphenamine can survive and retain their virulence for at least 48 weeks.

**Dietary Supplements of Vitamin $B_{12}$ in Growth Failure in School Children.** Wetzel, N. C., Hopwod, H. H., Kuechle, M. E., and Grueninger, R. M. *J. Clin. Nutr. 1*:17 (1952). Growth failure in children may pass unnoticed so long as the children attend school regularly and participate in regular activities. It is only when sequential data on weight and height are plotted as a record of the child's growth and development that retarded growth is evident. What is thus revealed is an entity at work which lowers physique, lessens physical vigor, and slows down the progress of all growth and development. Evidence over the years has given validity to the existence of growth retardation and of its hampering effect upon academic progress and achievement.

The authors studied the Grid records of some 4500 children in a particular school system. Forty children were then selected as controls and treated subjects for an evaluation of the effects of daily oral supplements of 10 micrograms of vitamin $B_{12}$ on the growth rate. A tabulation of results showed that 16 of 20 children with growth failure who received the supplement for 16 weeks showed a positive response. The mean gain in rate of growth for all 20 children was 0.60. This means that they increased in rate of growth the equivalent of 6 months over a year period. In other words, their rate of growth with supplementation was 1.5 times their prior rate of growth. In a group receiving the supplement for 6 weeks 7 of 16 showed a positive response with a mean increase in growth rate of 0.40. In contrast, 4 children with growth failure but not receiving a supplement showed a mean loss in growth rate of 0.13, and 20 children having no growth failure and not receiving supplements showed no significant deviation from their prior growth rate.

The authors, therefore, concluded that vitamin $B_{12}$ exerts a growth promoting effect when given as a dietary supplement to children showing evidence of growth failure. Individual rates were increased much more than the mean in several cases. Subjective signs of improvement were noted by physicians, nurses, teachers and parents. Behavior, attitude, and scholastic work improved; interest and attention was greater, and there was less strain and fatigue. The authors felt that vitamin $B_{12}$ probably acted by providing a marshaling effect upon a variety of metabolic derangements rather than meeting a specific dietary deficiency.

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